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(54) Title: SULPHYDRYL COMPOUNDS IN COMBINATION WITH SULPHONE OR SULPHONAMIDE COMPOUNDS FOR USE IN MICROBIAL INFLAMMATORY DISEASES

(57) Abstract: The present invention discloses various compositions and methods for co-administration of one or more sulfa compounds or pharmaceutically acceptable salts thereof, and one or more sulphydryl compounds in the treatment or prevention of disease, wherein the disease has in whole or part microbial and/or inflammatory origins.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 03/03538

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7 A61K31/095 A61K31/10 A61K31/18 A61K31/145 A61K31/198					
A61K31/20 A61K31/385 A61K31/426 A61P29/00 A61P31/00					
According to International Patent Classification (IPC) or to both national classification and IPC					
B. FIELDS SEARCHED					
Minimum documentation searched (classification system followed by classification symbols)					
IPC 7 A61K A61P					
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched					
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)					
EPO-Internal, BIOSIS, CHEM ABS Data, WPI Data, PAJ, EMBASE, PASCAL, SCISEARCH, CANCERLIT					
C. DOCUMENTS CONSIDERED TO BE RELEVANT					
Category *	Citation of document, with indication, where appropriate, of the relevant passages				Relevant to claim No.
X	WO 02 03972 A (WUELFERT ERNEST ; SALOMON ANDREW MARC (GB); ATKINSON ANTHONY (GB);) 17 January 2002 (2002-01-17) page 4, line 24 – line 27 page 5, line 2 – line 22 page 6, line 15 – line 19 page 7, line 2 – line 12 page 8, line 18 – line 22 claims 6,13,15,17 ----- WO 99 61004 A (MEDICAL RESEARCH INST) 2 December 1999 (1999-12-02) page 2, line 19 – line 20 page 3, line 25 – line 26 page 8, line 32 – page 9, line 3 ----- -----				1-5,8, 11-15
X					1,5,8,9, 11-13
					-/-
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.			<input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : <ul style="list-style-type: none"> "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed 					
*T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention					
*X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone					
*Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.					
*& document member of the same patent family					
Date of the actual completion of the international search			Date of mailing of the international search report		
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European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016			Albrecht, S		

INTERNATIONAL SEARCH REPORT

Internat'l Appl. No
PCT/IB 03/03538

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 15 December 1998 (1998-12-15) WALMSLEY SHARON L ET AL: "A randomized trial of N-acetylcysteine for prevention of trimethoprim-sulfamethoxazole hypersensitivity reactions in Pneumocystis carinii pneumonia prophylaxis (CTN 057)" Database accession no. PREV199900068991 XP002264341 abstract & JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES AND HUMAN RETROVIROLOGY, vol. 19, no. 5, 15 December 1998 (1998-12-15), pages 498-505, ISSN: 1077-9450</p> <p>---</p>	16,17
Y	<p>GB 550 011 A (MORRIS SELIG KHARASCH;OTTO REINMUTH; LILLY CO ELI) 18 December 1942 (1942-12-18) page 1, line 22 - line 33 column 1, line 43 -column 2, line 2</p> <p>---</p>	1-17
Y	<p>BUDINSKY R ET AL: "DAPSONE-INDUCED HEMOLYTIC ANEMIA PROTECTIVE EFFECT OF SULFHEDRYL AGENTS" FASEB JOURNAL, vol. 2, no. 4, 1988, page ABSTRACT 2934 XP009022689 72ND ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, LAS VEGAS, NEV ISSN: 0892-6638 the whole document</p> <p>---</p>	1-17
Y	<p>DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; COLEMAN, MICHAEL D. ET AL: "Monitoring antioxidant effects using methaemoglobin formation in diabetic erythrocytes" retrieved from STN Database accession no. 137:118960 XP002264339 abstract & BRITISH JOURNAL OF DIABETES & VASCULAR DISEASE (2001), 1(1), 88-92 ,</p> <p>---</p> <p>-/-</p>	1-17

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 03/03538

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>RIEDER M J ET AL: "SULFONAMIDE HYPERSENSITIVITY REACTIONS REVERSAL OF HYDROXYLAMINE TOXICITY BY N ACETYL CYSTEINE IN LYMPHOCYTES OF PATIENTS AND NORMAL VOLUNTEERS" PEDIATRIC RESEARCH, vol. 23, no. 4 PART 2, 1988, page 263A XP009022686 JOINT MEETING OF THE AMERICAN PEDIATRIC SOCIETY AND THE SOCIETY FOR PEDIATRIC RESEARCH, WASHINGTON, ISSN: 0031-3998 the whole document</p> <p>---</p>	1-17
Y	<p>DATABASE CA 'Online' CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; RIEDER, MICHAEL J. ET AL: "Toxicity of sulfonamide-reactive metabolites in HIV-infected, HTLV-infected, and noninfected cells" retrieved from STN Database accession no. 122:230194 XP002264340 abstract & JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES AND HUMAN RETROVIROLOGY (1995), 8(2), 134-40 ,</p> <p>---</p>	1-17
Y	<p>WO 01 41772 A (ZOLOTOY ALEXANDER ;BAIN ALLEN I (CA); IMMUNE NETWORK RES LTD (CA);) 14 June 2001 (2001-06-14) page 1, paragraph 3 claims 1,10-13</p> <p>---</p>	14-17
Y	<p>WO 93 24118 A (UNIV BRITISH COLUMBIA) 9 December 1993 (1993-12-09) cited in the application page 1, line 16 -page 2, line 12 claim 1</p> <p>---</p>	14-17
Y	<p>WO 96 14838 A (VIVORX PHARMACEUTICALS INC) 23 May 1996 (1996-05-23) page 1, line 2 - line 12 page 2, line 29 - line 31</p> <p>---</p>	14-17

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 14-17 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: 1-5,8,9,11-17 (all in part) because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-5,8,9,11-17 (all in part)

In view of the expressions "derivatives", "analogues", "metabolites", "metabolic precursors" and "prodrugs", present claims 1, 3-5, 8, 9, 11-17 relate to an extremely large number of possible compounds, in particular since the claimed compound(s) is/are only defined by one chemical moiety (sulphone, sulphonamide, sulphhydryl). In fact, these claims are defined in such a way that a lack of clarity and/or conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search for these claims as well as for claim 2 has been restricted to the expressions "sulphone" and "sulphonamide" and to 4,4'-diaminodiphenylsulphone (mentioned in claim 3 and in the examples) and sulphamethoxazole (indicated on page 2, 1.9 of the description), as far as the sulphone/sulphonamide compound is concerned. The same objection applies to the sulphhydryl compound, for which the search has been limited to the specific compounds indicated in claim 2 and to dihydrolipoic acid (indicated on page 7 of the description).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Internat'l Appl. No.
PCT/IB 03/03538

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